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Quality of Synthetic Peptide Drugs: Key Influencing Factors and Control Measures

Peptide drugs are widely used in clinical treatment, and consistent quality and controllable safety are central to their industrial production. The quality of synthetic peptides is influenced by multiple factors, including raw materials, reagents, processes, equipment, and purification; any variation can lead to reduced purity, excessive impurities, or decreased activity, thereby affecting therapeutic efficacy and patient safety. Recently, researchers have systematically identified the key factors affecting the quality of synthetic peptide drugs and established a comprehensive quality control system, providing a scientific basis for ensuring product consistency and enhancing production stability.

I. Research Background

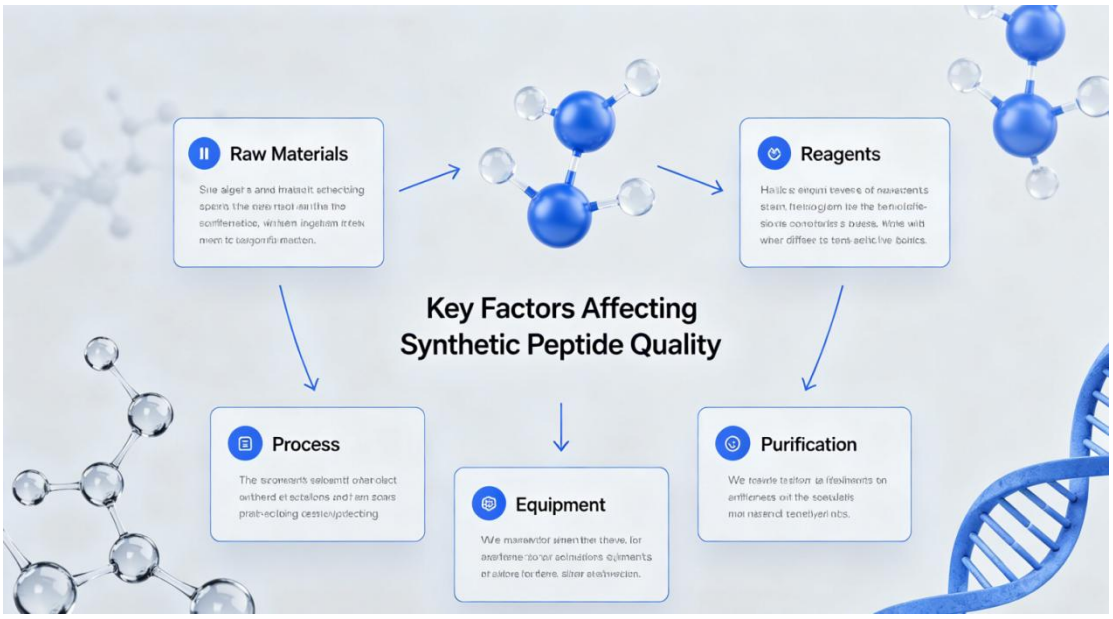
Due to their high specificity and low incidence of side effects, peptide drugs have become a key focus in new drug development, with solid-phase synthesis (SPPS) and liquid-phase synthesis (LPPS) serving as the mainstream preparation techniques. However, production commonly faces challenges such as fluctuations in raw material purity, unstable reagent quality, deviations in process parameters, and insufficient purification efficiency. These issues can easily lead to problems such as amino acid deletions or insertions, residual protecting groups, racemization, and byproduct formation, resulting in batch-to-batch quality variations, reduced stability, and even safety risks. Therefore, comprehensively identifying quality-affecting factors and establishing a standardized control system are urgent requirements for the industrial production of peptide drugs.

II. Research Objectives and Significance

This study aims to systematically analyze the impact of raw materials, reagents, reaction conditions, equipment, and purification processes on the quality of synthesized

peptides, identify critical control points, and establish a quality control and batch consistency management plan covering the entire production process. The findings will help companies precisely control production processes, optimize process parameters, and reduce the risk of impurities, thereby enhancing the purity, stability, and bioactivity of peptide drugs and ensuring their safety and efficacy for clinical use. At the same time, they will provide a reference for the industry to establish quality standards and promote the high-quality development of peptide drugs, helping to enhance the international competitiveness of domestically produced peptide drugs.

III. Research Content



The research team conducted a detailed analysis of the factors influencing peptide synthesis quality and corresponding control measures across five key areas: starting materials, process control, equipment-based purification, quality testing, and system management. Regarding raw materials, amino acid purity must be ≥98%, and the quality of protecting groups (Fmoc/Boc) must be strictly controlled to avoid batch-to-batch variations. For reagents, the purity and moisture content of activators (HBTU/DIC) and solvents (DMF/DMAc) must be controlled to minimize side reactions. In terms of process control, temperature (temperature difference ≤ ±0.5°C), pH, and reaction time must be precisely controlled, while deprotection conditions should be optimized to reduce the risk of racemization and degradation. Automated synthesis

systems are employed to ensure precise temperature control and timing; purification primarily utilizes RP-HPLC, with column temperature and flow rate optimized to enhance impurity separation efficiency. For quality control, LC-MS, HPLC, microbiological, and toxicological testing are employed to precisely monitor purity, impurities, activity, and stability. Through methods such as SPC, DOE, and Six Sigma, batch consistency and process traceability are achieved, ensuring that batch-to-batch purity is ≥98%, impurities are ≤0.3%, and stability meets specifications.

IV. Conclusions and Outlook

Research indicates that the quality of synthetic peptide drugs is determined by multiple factors, including raw materials, reagents, processes, equipment, and purification. Any deviation in these areas can compromise product purity, stability, and safety. By strictly controlling the quality of raw materials and reagents, precisely managing process parameters, optimizing purification protocols, adopting high-efficiency detection technologies, and establishing a standardized quality management system, it is possible to effectively ensure batch-to-batch consistency and stable product quality. In the future, quality control for peptide drugs will continue to focus on refined process optimization, intelligent process monitoring, green production technologies, and precise traceability of impurities. By thoroughly analyzing the mechanisms of impurity formation and refining quality standards and process validation systems, we will drive the development of synthetic peptide drugs toward higher purity, greater stability, enhanced safety, and lower costs. This will provide superior therapeutic options for clinical use and support the high-quality upgrading of the peptide industry.